# WEST Search History

DATE: Monday, March 24, 2003

| Set Name side by side | Query | Hit Count | Set Name result set |
|---|---|---|---|
| | *DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR* | | |
| L10 | (l2 or l3) near5 (depression or antidepress$6) | 63 | L10 |
| L9 | (l2 or l3) near10 (depression or antidepress$6) | 95 | L9 |
| L8 | (l2 or l3) near10 (depressi$4 or antidepress$6) | 99 | L8 |
| L7 | (l2 or l3) same l5 | 26 | L7 |
| L6 | l3 same l5 | 17 | L6 |
| L5 | dissoc$6 or refract$4 near3 depressi$4 | 65897 | L5 |
| L4 | l1 same L3 | 0 | L4 |
| L3 | nalmefene or naloxone or naltrexone or nalbuphine or thebaine | 2688 | L3 |
| L2 | (opiate$1 or opioid$1) near3 antagonis$4 | 1503 | L2 |
| L1 | (depressi$4 or antidepress$4) near5 dissocia$6 | 22 | L1 |

END OF SEARCH HISTORY

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FILE 'HOME' ENTERED AT 07:40:09 ON 24 MAR 2003

=> s (depress? or antidepress?)(5a)dissoc?
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
index.  Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> file caplus,biosis,medline,drugu,embase
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                   0.42       0.42

FILE 'CAPLUS' ENTERED AT 07:41:01 ON 24 MAR 2003
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FILE 'BIOSIS' ENTERED AT 07:41:01 ON 24 MAR 2003
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FILE 'MEDLINE' ENTERED AT 07:41:01 ON 24 MAR 2003

FILE 'DRUGU' ENTERED AT 07:41:01 ON 24 MAR 2003
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FILE 'EMBASE' ENTERED AT 07:41:01 ON 24 MAR 2003
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=> s (depress? or antidepress?)(5a)dissoc?
L1          776 (DEPRESS? OR ANTIDEPRESS?)(5A) DISSOC?

=> s (opioid? or opiate?)(2a)antagonist? or nalmefene or naloxone or naltrexone or
nalbuphine or thebaine
L2       124651 (OPIOID? OR OPIATE?)(2A) ANTAGONIST? OR NALMEFENE OR NALOXONE
                OR NALTREXONE OR NALBUPHINE OR THEBAINE

=> s l1 and l2
L3           12 L1 AND L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4             8 DUP REM L3 (4 DUPLICATES REMOVED)

=> d 1-8 bib,ab

L4   ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2003 ACS
AN   2003:133037  CAPLUS
DN   138:163579
TI   Treatment of refractory depression with an opiate
     antagonist and an antidepressant
IN   Glover, Hillel; Chrisman, Deborah
PA   USA
SO   PCT Int. Appl., 27 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
```

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003013524 | A1 | 20030220 | WO 2002-US24430 | 20020802 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-925190 A 20010809

AB An antidepressant or a pharmaceutically acceptable salt thereof, and an **opiate antagonist** or a pharmaceutically acceptable salt thereof, are used to treat refractory **depression** characterized by **dissocn**. Two patients scoring high on the Beck Depression Inventory and on the Glover Numbing Scale were treated with the **opiate antagonist nalmefene** and with SAM-E or venlafaxine as antidepressant.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 8 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2002364548 EMBASE
TI [Pain perception in self-injurious syndrome].
PERCEPCION DEL DOLOR EN EL SINDROME DE COMPORTAMIENTO AUTOLESIVO.
AU Mendoza Y.; Pellicer F.
CS Dr. F. Pellicer, Subdireccion de Neurociencias, Inst. Nac. Psiq. Ramon de la Fuente, Calzada Mexico-Xochimilco 101, San Lorenzo Huipulco 14370, Mexico. pellicer@imp.edu.mx
SO Salud Mental, (2002) 25/4 (10-16).
Refs: 62
ISSN: 0185-3325 CODEN: SAMEF5
CY Mexico
DT Journal; Article
FS 008 Neurology and Neurosurgery
032 Psychiatry
037 Drug Literature Index
LA Spanish
SL English; Spanish
AB Deliberate physical harm to one's own body without the intention of dying is a frequent and difficult to treat psychiatric phenomenon. Self-injurious behavior (SIB) is a self-destructive behavior causing obvious tissue damage. In different psychiatric conditions such as psychotic states, mentally retardation, and personality disorders, SIB is a paradoxical sign since it would seem that the mechanisms related to pain, whose purpose is the detection of an actual or potential damage to individual integrity, would cause the opposite effect: direct tissue damage. In this work we argue that SIB is due to a dysfunction of the cerebral limbic structures involved in the cognitive and emotional processing of pain. Such dysfunction constitutes an anomaly in the integration of pain as a conscious experience whereby it is conceived as an unpleasant sensation. We suppose that such disturbed pain perception can be considered as a consequence, manifestation, or symptom of a problem in self-consciousness, resulting from the interaction between biological and environmental factors. Studies in animals SIB has been shown to develop in rhesus monkeys reared in socially deprived environments. The

severity of SIB correlates with the extent of isolation in terms of total duration and age at which it began. In socially deprived juvenile rhesus monkeys, D-amphetamine elicits SIB, and a dose-dependent increase of norepinephrine in cerebro-spinal fluid (CSF). Rodents with a neonatal chemical denervation of dopamine terminals, bite themselves when administered apomorphine or L-dopa. This response seems to be mediated through a D1-receptor supersensitivity. Adult rats, when administered high doses of caffeine, pemoline or amphetamine, display SIB. The effects of dopamine, NMDA, opiate, and serotonin related agents on acute metamphetamine induced SIB in mice, while D1 antagonists and 5HT precursors reduced the incidence of SIB, and NMDA antagonist completely removed it; neither D2 antagonists nor **naloxone** affected SIB. It is possible to generate SIB in rats after inducing peripheral nerve lesions and inflammation process in a limb. This behavior is enhanced by electric stimulation of the cingulum or by the destruction of the ventral tegmental area (VTA), while the electric stimulation of VTA diminishes it. In conclusion, dopaminergic system plays an important role on the genesis of SIB, particularly on some brain structures related to the affective-motivational components of pain processing such as VTA, anterior cingulate cortex (ACC), and anterior thalamus. SIB in mentally retarded patients About 15 to 20% of the patients with learning disabilities or mentally retardation who attend health or social services show SIB. One hypothesis suggests that severe SIB is associated with a release of endorphins resulting in relative analgesia and a rewarding mood state. Thus, a cycle of escalating tissue damage may follow since SIB is necessary to maintain a chronic release of endogenous opiods. This hypothesis is supported by the observation that **opiate antagonists** attenuate severe SIB in a subgroup of autistic patients. The dopaminergic system is believed to be responsible for SIB on Lesch-Nyhan syndrome through a receptor supersensitivity. It can be proposed that these patients have a dopaminergic supersensitivity of D1 receptors in the cingulate bundle of the prefrontal cortex that causes a dysfunction in the cognitive processes related to pain. SIB in personality disorders Self-injurious behavior occurs in 70 to 80% of patients who meet DSM-IV criteria for borderline personality disorder (BPD). In 1990, Gardner found in BPD patients that lower levels of CSF 5-HIAA were significantly associated with a history of suicide attempts and SIB. Moreover, the degree of SIB was significantly correlated with impulsivity, chronic anger and somatic anxiety. A significant negative correlation was found with the number of platelet imipramine receptor sites. BPD patients with SIB showed a blunted prolactin response to meta-clorophenylpiperazine that appears to be in inverse relation with the frequency of physical and sexual abuse in infancy. About 30 to 40% of BPD patients report that they do not feel pain during SIB and show lower experimental pain ratings than BPD patients who do experience pain during SIB. They also exhibit higher ratings of **depression**, anxiety, impulsiveness, and **dissociation**, as well as suicide attempts and childhood sexual abuse. The abnormal perception of pain in this group of patients may be related to a tendency to show dissociative symptoms. Thus, EEG theta activity in patients that do not feel pain during SIB, is significantly correlated with the Dissociative Experience Scale score. Pain perception and dissociation Theta rhythm is recorded in hypnotic states as well as during anticipation and control of painful stimulation in healthy individuals. This activity seems to be generated in medial prefrontal cortex and cingulate cortex, the same structures involved in the affective component of pain. Possitron emission tomography revealed significant changes in pain evoked activity within ACC, consistent with the perceived unpleasantness in normal subjects under pain stimulus. The three main dimensions of pain (intensity sensation, unpleasantness and secondary affect) are processed in brain structures that receive serial and parallel

information. Spinal pathways to limbic structures and medial thalamic nuclei provide direct input to brain areas involved in affect. Another pathway is through somato-sensorial thalamic and cortical areas and then by a corticolimbic pathway. Both arrive to the same cortical and subcortical structures of the cingulum. This structure integrates nociceptive stimuli with contextual information and memory to provide the adequate cognitive mediation of pain. In 1998, Sierra and Berrios proposed that the state of increased alertness in despersonalization results from an activation of prefrontal attentional systems (right dorsolateral prefrontal cortex) and a reciprocal inhibition of the ACC, leading to experiences of "mind emptiness" and "indifference to pain". On the other hand, left prefrontal mechanisms would inhibit the amygdala resulting in a dampened autonomic output. Dissociative symptoms and SIB in BPD patients are common clinical signs. Besides, BPD patients show hypometabolism in prefrontal cortical areas and ACC. It is proposed that the same structures that lead to dissociative states may change the perception of pain by cognitive processes. Conclusions The authors hypothesize that the structures involved in processing the cognitive component of pain (anterior cingulate and medial prefrontal cortex) are altered in those patients who exhibit self-injurious behavior. The adequate physiological response to a noxious stimulus, requires that the individual perceives himself in order to maintain his integrity. Therefore, the alteration of pain perception could be the consequence of problem in self-consciousness.

L4 ANSWER 3 OF 8 MEDLINE
AN 1999270364 MEDLINE
DN 99270364 PubMed ID: 10340539
TI The effects of intravenous naltrindole and naltrindole 5'-isothiocyanate on sufentanil-induced respiratory depression and antinociception in rats.
AU Verborgh C; Meert T F
CS Departement Anesthesiologie, Akademisch Ziekenhuis Vrije Universiteit Brussel, Belgium.
SO PHARMACOLOGY, BIOCHEMISTRY AND BEHAVIOR, (1999 May) 63 (1) 175-83. Journal code: 0367050. ISSN: 0091-3057.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199907
ED Entered STN: 19990806
Last Updated on STN: 19990806
Entered Medline: 19990728
AB Although the interactions between the mu- and the delta-opiate receptor subtypes are well documented with regard to supraspinal analgesia, less is known about the mutual interactions on respiratory depression. To clarify the functional interactions between both opiate receptor subtypes with regard to antinociception and respiratory depression, male Wistar rats were intravenously injected with 2.5 microg/kg of the mu-opiate agonist sufentanil and subsequently intravenously challenged with the delta antagonist naltrindole (NTI) or naltrindole 5'-isothiocyanate (5'-NTII), a delta-2 antagonist. Antinociception was measured by means of the tail-flick latency, and respiratory depression was evaluated by means of analysis of PaCO2, PaO2, and oxygen saturation. To quantify the antagonistic properties of NTI and 5'-NTII, mean areas under the curve were calculated for groups treated with sufentanil, control vehicle, and sufentanil plus a dose of the antagonists. NTI, but not 5'-NTII, antagonized the sufentanil-induced antinociception at 10 mg/kg NTI. Below this dose the effects were inconsistent. The sufentanil-induced hypercapnia and hypoxia were diminished with 10 mg/kg NTI or 5'-NTII. These data indicate that NTI antagonizes the sufentanil-induced

antinociception and respiratory **depression** in rats. A **dissociation** between the antinociception and respiratory **depression** following intravenous sufentanil could be obtained with 10 mg/kg 5'-NTII pointing to different regulatory effects of opiate delta receptor subtypes on mu-opiate agonist-induced behavioral effects.

L4 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
AN 1989:625178 CAPLUS
DN 111:225178
TI On the selectivity of intravenous .mu.- and .kappa.-opioids between nociceptive and non-nociceptive reflexes in the spinalized rat
AU Parsons, Chris G.; Headley, P. Max
CS Sch. Med. Sci., Univ. Bristol, Bristol, BS8 1TD, UK
SO British Journal of Pharmacology (1989), 98(2), 544-51
CODEN: BJPCBM; ISSN: 0007-1188
DT Journal
LA English
AB In electrophysiol. expts. in spinalized, .alpha.-chloralose anesthetized rats, opioids and anesthetics were tested i.v. on the responses of individual motoneurones to alternating noxious (heat or pinch) and nonnoxious (tap or vibration) stimuli. On cells that were sensitive to low dose of .mu.-opioids, both fentanyl (0.5-4 .mu.g/kg i.v.) and morphine (0.5 mg/kg i.v.) selectivity reduced reflexes to noxious stimuli to a greater degree than reflexes to nonnoxious stimuli. In contrast, on cells that were relatively resistant to these agonists, the higher doses required to reduce nociceptive reflexes (fentanyl 8 .mu.g/kg i.v.; morphine 1-8 mg/kg i.v.) depressed nonnociceptive reflexes to a similar degree. A similar spectrum of selectivity was seen with U-50,488 (0.5-16 mg/kg i.v.) although statistically significant selective depression of reflexes was only evident at the lowest dose tested (0.5 mg/kg i.v.). All effects of U-50,488 were readily reversed by low doses of the **opioid antagonist, naloxone** (10-100 .mu.g/kg i.v.). The dissociative anesthetic/PCP ligand ketamine (0.5-4 mg/kg i.v.) was similar in having selective actions at low doses on sensitive cells but nonselective actions when higher doses were required. In contrast, the general anesthetics methohexitone (4 mg/kg i.v.) and alphadolone/alphaxalone (1 mg/kg i.v.) were consistently nonselective between reflexes to noxious and nonnoxious stimuli. .alpha.-Chloralose (20-40 mg/kg i.v.) had very little effect on reflexes to any of the synaptic inputs tested. The sensitivity of nociceptive reflexes to **depression** by opioids and **dissociative** anesthetics thus dets. the selectivity of these agents between nociceptive and nonnociceptive reflexes. The same is not true for the general anesthetics tested. Taken together with previous findings that .kappa.- as well as .mu.-agonists reduce thermal and mech. nociceptive reflexes in parallel, these results indicate a general similarity of spinal .mu.- and .kappa.-opioid actions in the spinal cord of the rat.

L4 ANSWER 5 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1989:164045 BIOSIS
DN BA87:86146
TI RECEPTOR BINDING OF TRITIATED **NALOXONE** BENZOYLHYDRAZONE A REVERSIBLE KAPPA AND SLOWLY DISSOCIABLE MU OPIATE.
AU PRICE M; GISTRAK M A; ITZHAK Y; HAHN E F; PASTERNAK G W
CS MEMORIAL SLOAN-KETTERING CANCER CENTER, 1275 YORK AVENUE, NEW YORK, N.Y. 10021.
SO MOL PHARMACOL, (1989) 35 (1), 67-74.
CODEN: MOPMA3. ISSN: 0026-895X.
FS BA; OLD
LA English

AB In standard 3H-opioid binding assays, the benzoylhydrazone derivative of **naloxone** (6-desoxy-6-benzoylhydrazido-N-allyl-14-hydroxydihydronormorphinone; NalBzoH) inhibited .mu., .kappa., and .delta. binding at nanomolar concentrations. At concentrations as low as 1 nM, it also produced a wash-resistant inhibition of opioid binding. [3H]NalBzoH binding typically gave a ratio of total to nonspecific binding of 8:1. Binding reached steady state levels by 1 hr and was linear with tissue concentration. [3H]NalBzoH labeled two classes of sites. The binding to one was easily reversible whereas the other was not and was termed pseudoirreversible. At 25.degree., almost 90% of [3H]**naloxone** binding and approximately 60-75% of [3H]NalBzoH binding dissociated over 90 min. However, the remainder of [3H]NalBzoH binding, corresponding to pseudoirreversible binding, remained constant over the next 5 hr at 25.degree. and additional studies suggested a dissociation half-life of approximately 24 hr. Competition studies indicated that the reversible binding corresponding to neither .mu. nor .delta. binding and may represent a novel subtype of .kappa. receptor. Pseudoirreversible binding was predominantly to a combination of both .mu.1 and .mu.2 receptors. Despite its extremely slow rate of dissociation, pseudoirreversible binding was not covalent inasmuch as lowering the pH to 5 or adding the GTP analog 5'-guanylylimidodiphosphate [Gpp(NH)p] completely dissociated prebound [3H]NalBzoH. The ability of Gpp(NH)p to dissociate pseudoirreversible [3H]NalBzoH binding raised the possibility that the slow rate of dissociation was related to interactions with a guanine neucleotide-binding protein.

L4 ANSWER 6 OF 8 DRUGU COPYRIGHT 2003 THOMSON DERWENT
AN 1984-23736 DRUGU P
TI Respiratory **Depression** and Analgesia Induced by Neurotensin: **Dissociation** with **Naloxone**. (Esp.).
AU Pazos A; Lopez M; Florez J
LO Santander, Spain
SO J.Pharmacol. (14, No. 4, 543, 1983)
CODEN: JNPHAG
AV Departamento de Farmacologia y Terapeutica, Fac. Medicina, Univ. Santander, Ctr. Med. Nac. ''Valdecilla'', Santander, Spain.
LA French
DT Journal
FA AB; LA; CT
FS Literature
AB Rats were treated with intracerebroventricular neurotensin. Respiratory depression was produced. Respiratory frequency was affected in a dose-dependent manner until apnea occurred. The amplitude of respiration was affected secondarily. The ED50 was 137.5 nmol. Where depression did not exceed 50%, i.v. **naloxone** completely antagonized this effect. The analgesic effect of neurotensin (ED50 2.3 nmol) was not antagonized by **naloxone**. It was suggested that respiratory depression due to neurotensin involved indirect activation of opiate receptors. (congress).

L4 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 1983:155092 CAPLUS
DN 98:155092
TI **Dissociation** of morphine's analgesic respiratory **depressant** actions
AU Ling, Geoffrey S. F.; Spiegel, Katharyn; Nishimura, Stephen L.; Pasternak, Gavril W.
CS Cotzias Lab. Neuro-Oncol., Mem. Sloan-Kettering Cancer Cent., New York, NY, 10021, USA
SO European Journal of Pharmacology (1983), 86(3-4), 487-8

CODEN: EJPHAZ; ISSN: 0014-2999
DT Journal
LA English
AB In rats, naloxonazine (10 mg/kg, i.v.) (an irreversible **opiate antagonist** selective for .mu.1 sites) effectively and completely blocked the analgesic activity of morphine (I) [57-27-2] (3.5 mg/kg, i.v.) without affecting its respiratory depressant action.

L4 ANSWER 8 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 1981:177795 BIOSIS
DN BA71:47787
TI COMPARATIVE STUDY OF THE ACTIONS OF **NALOXONE** AND ALMITRINE ON FENTANYL ANALGESIA IN THE ANESTHETIZED DOG EFFECTS ON THE MUZZLE OPENING REFLEX AND BLOOD GASES.
AU DAUTHIER C; GAUDY J H; WILLER J C
CS LAB. ANESTHESIOL., HOP. ROTHSCHILD, 33 BLVD. PICPUS-75012 PARIS, FR.
SO ANN ANESTHESIOL FR, (1980) 21 (4), 421-430.
CODEN: AANFAE. ISSN: 0003-4061.
FS BA; OLD
LA French
AB The search for a technique to **dissociate** the analgesia and ventilatory **depression** of central analgesics led to a comparison of the effects of **naloxone**, a specific morphinomimetic antagonist, with almitrine, a ventilatory stimulant with a peripheral action, on muzzle opening reflex and blood gases. Five male dogs (beagles, 1 yr old), anesthetized with Alfetesine were treated separately with the 2 drugs used alone and after fentanyl analgesia (injection of fractionated doses up to the threshold of apnea). The association of the 2 drugs was tested in the dog after analgesia. The parameters studied were muzzle opening reflex [MOR], as an indication of analgesia and blood gases, and were observed for 45 min, including 15 min control. The i.v. injection of 1.2 mg **naloxone** increased the surface area of muscle potentials with a maximum of 7% (P 0.001) at the 15th min. No significant change in blood gases was seen. In the same dogs given fentanyl analgesia, **naloxone** reversed respiratory depression and had a stimulatory effect on MOR reaching 7% (P 0.001) at the 30th min. The effects of 1 mg/kg of almitrine were characterized by a fall in MOR for a period equal to that of the study and a minumum of 7.8% (P 0.001) at the 20th min. At the same time, marked ventilatory stimulation was seen. P[partial pressure]O2 rose by 22.7% (P 0.02) at the 5th min. PCO2 fell during the 30 min studied with a minimum of 39.5% (P 0.01) at the 20th min. Almitrine did not antagonize the depression of MOR caused by fentanyl but reversed the respiratory depression of the analgesic, increasing PO2 by 26% (P 0.01) and decreasing PCO2 by 25.7% (P 0.01). The combination of both drugs cancelled out the abolition of the reflex by fentanyl then facilitated it up to 24.7% (P 0.001) in comparison with the animal not receiving any analgesic. The ventilatory action of almitrine was not potentialized by **naloxone**. In the absence of any emergency, the choice of **naloxone** as an antagonist of ventilatory depression of central analgesics should not be preferential to avoid the rebound effect.

L4 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 2003:133037 CAPLUS
DN 138:163579
TI Treatment of refractory depression with an **opiate antagonist** and an antidepressant
IN Glover, Hillel; Chrisman, Deborah
PA USA
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-44
ICS A61K031-55; A61K031-135; A61K031-335
CC 1-11 (Pharmacology)
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2003013524 | A1 | 20030220 | WO 2002-US24430 | 20020802 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-925190 A 20010809

AB An antidepressant or a pharmaceutically acceptable salt thereof, and an **opiate antagonist** or a pharmaceutically acceptable salt thereof, are used to treat refractory **depression** characterized by **dissocn**. Two patients scoring high on the Beck Depression Inventory and on the Glover Numbing Scale were treated with the **opiate antagonist nalmefene** and with SAM-E or venlafaxine as antidepressant.

ST refractory **depression dissocn opiate antagonist antidepressant**; venlafaxine **nalmefene** treatment refractory depression; SAM E **nalmefene** treatment refractory depression

IT Ketones, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino, as antidepressants; refractory depression treatment with **opiate antagonist** and antidepressant)

IT 5-HT antagonists
(as antidepressants; refractory depression treatment with **opiate antagonist** and antidepressant)

IT Fruit and vegetable juices
Milk
(as **opiate antagonist** carrier; refractory depression treatment with **opiate antagonist** and antidepressant)

IT Mental disorder
(**depression**, refractory with **dissocn.**; refractory **depression** treatment with **opiate antagonist** and antidepressant)

IT Amines, biological studies

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(keto, as antidepressants; refractory depression treatment with **opiate antagonist** and antidepressant)

IT Emotion
(lack of feeling, evaluation for; refractory depression treatment with **opiate antagonist** and antidepressant)

IT Drug delivery systems
(oral; refractory depression treatment with **opiate antagonist** and antidepressant)

IT Antidepressants
Human
**Opioid antagonists**
(refractory depression treatment with **opiate antagonist** and antidepressant)

IT Beverages
(sweetened, as **opiate antagonist** carrier; refractory depression treatment with **opiate antagonist** and antidepressant)

IT Antidepressants
(tricyclic; refractory depression treatment with **opiate antagonist** and antidepressant)

IT Biological transport
(uptake, dual reuptake inhibitors, as antidepressants; refractory depression treatment with **opiate antagonist** and antidepressant)

IT **Opioid antagonists**
(.kappa.-**opioid**; refractory depression treatment with **opiate antagonist** and antidepressant)

IT 50-48-6, Amitriptyline 50-49-7, Imipramine 72-69-5, Nortriptyline 23047-25-8, Lofepramine 29908-03-0, SAM-E 34911-55-2, Bupropion SR 54739-18-3, Fluvoxamine 54910-89-3, Fluoxetine 59729-33-8, Citalopram 61869-08-7, Paroxetine 71620-89-8, Reboxetine 79617-96-2, Sertraline 83366-66-9, Nefazodone 85650-52-8, Mirtazapine 93413-69-5, Venlafaxine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as antidepressant; refractory depression treatment with **opiate antagonist** and antidepressant)

IT 7732-18-5, Water, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as **opiate antagonist** carrier; refractory depression treatment with **opiate antagonist** and antidepressant)

IT 115-37-7, **Thebaine** 465-65-6, **Naloxone** 16590-41-3, **Naltrexone** 20594-83-6, **Nalbuphine** 55096-26-9, **Nalmefene**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as **opiate antagonist**; refractory depression treatment with **opiate antagonist** and antidepressant)

IT 50-67-9, Serotonin, biological studies 51-61-6, Dopamine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enhancers or reuptake inhibitors, as antidepressants; refractory depression treatment with **opiate antagonist** and antidepressant)

IT 51-41-2, Norepinephrine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enhancers or selective reuptake inhibitors, as antidepressants;

refractory depression treatment with **opiate antagonist** and antidepressant)

IT 9001-66-5, Monoamine oxidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, as antidepressants; refractory depression treatment with **opiate antagonist** and antidepressant)

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Dante; US 5512593 A 1996 CAPLUS
(2) Dante; US 5856332 A 1999 CAPLUS